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SOURCE: 39 FR 18944, May 30, 1974, unless otherwise noted.

Subpart A—Definitions; Interpretations; Requirements

§ 436.1 Sterility requirements of items packaged with sterile antibiotic drugs.

(a) *Diluents packaged in combination with sterile antibiotic drugs.* If a sterile antibiotic drug is packaged in combination with an immediate container of a diluent, the immediate container of diluent shall be sterile when tested by the method prescribed in § 436.20(e)(1).

(b) *Dispensers packaged in combination with sterile antibiotic drugs.* If a sterile antibiotic drug is packaged in combination with a dispenser, such dispenser shall be sterile when tested by the method prescribed in § 436.20(e)(1).

[39 FR 18944, May 30, 1974, as amended at 41 FR 46852, Oct. 26, 1976]

§ 436.2 Alternative assay methods.

Alternative assay methods (including automated procedures) employing the same basic chemistry or microbiology as the official methods described in this part and in the individual monographs of this chapter may be used, provided the results obtained are of equivalent accuracy. However, only the results obtained from the official methods designated in the individual monographs are conclusive.

Subpart B—Sterility Test Methods

§ 436.20 Sterility test methods and procedures.

(a) *Laboratory facilities.* The test must be performed using aseptic techniques in an area as free from contamination as is possible to achieve. Testing should not be conducted under direct exposure to ultraviolet light or in areas under aerosol treatment. Environmental tests to assess the suitability of testing conditions should be made frequently enough to assure the validity of test results.

(b) *Equipment and reagents*—(1) *Bacterial membrane filter.* The filter has a nominal porosity of 0.45 micron±0.02 micron, a diameter of approximately 47 millimeters, and a flowrate of 55 milliliters to 75 milliliters of distilled water passing each square centimeter of filter area per minute with a differential pressure of 70 centimeters of mercury at 25° C.

(2) *Penicillinase solutions.* When the amount of penicillinase to be used is specified in terms of Levy units, use a penicillinase solution standardized in terms of Levy units. One Levy unit of penicillinase inactivates 59.3 units of penicillin G in 1 hour at 25° C. and at a pH of 7.0 in a phosphate buffered solution of a pure alkali salt of penicillin G when the substrate is in sufficient concentration to maintain a zero order reaction.

(c) *Culture media.* Use ingredients that conform to the standards prescribed by the U.S.P. or N.F. In lieu of preparing the media from the individual ingredients, they may be made from dehydrated mixtures which, when reconstituted with distilled water, have the same or equivalent composition as such media and have growth-promoting buffering, and oxygen tension-controlling properties equal to or better than such media. The pH of each medium should be adjusted with 2*N* hydrochloric acid or sodium hydroxide